

## Claims

- 5 1. An isolated polypeptide comprising one or more of the amino acid motifs selected from the group consisting of a sequence with at least 80% identity to any of
- (a) P-L-X-D-X(35,75)-R-R-X(8)-[YF]-X(2)-R-X(6)-T
- 10 (b) C-X-D-X(3)-S-G-H-T
- (c) H-Y-[TS]-X-D-[VI]-X(3)-[FYI]-X(6)-F-X(2)-Y-H.
- 15 2. A polypeptide according to claim 1 that is derived from the group consisting of *Animalia*, *Alveolata* and *Kinetoplastida*.
3. A polypeptide according to claim 1 or 2 selected from the group comprising any of the SEQ ID No. 1 - 11 or at least 70% similarity thereto.
- 20 4. A polypeptide according to claim 1 or 2 comprising an amino acid sequence with at least 70 % similarity to any of the SEQ ID No. 12 - 22.
- 25 5. A polypeptide according to any one of the previous claims comprising an amino acid sequence with at least 20 % identity to any of the SEQ ID No. 12 - 22.
- 30 6. A polypeptide according to claim 5 comprising an amino acid sequence with at least 30 % identity to SEQ ID No. 12.

7. A polypeptide according to claim 5 comprising an amino acid sequence with at least 40 % identity to any of the SEQ ID No. 19 - 21.
- 5
8. A polypeptide according to any one of the claims 1 - 3 comprising an amino acid sequence with at least 22 % identity to SEQ ID No. 22.
- 10 9. A polypeptide according to any one of the claims 1 - 6 with sphingomyelin synthase activity.
10. A polypeptide according to any one of the claims 1 - 5 and 7 with ethanolamine phosphorylceramide synthase activity.
- 15
11. A polypeptide according to any one of the claims 1 - 5 and 8 with one or more of the activities selected from the group consisting of phosphatidylcholine:glycoprotein cholinephosphotransferase and phosphatidylcholine:glycolipid cholinephosphotransferase.
- 20
12. A nucleotide sequence selected from the group consisting of a nucleotide sequence coding for any of the amino acid sequences as described in claim 9 and an anti sense nucleotide sequence that is complementary thereto.
- 25
13. A nucleotide sequence selected from the group consisting of a nucleotide sequence coding for any of the amino acid sequences as described in claim 10 and an anti sense nucleotide sequence that is complementary thereto.
- 30 14. A nucleotide sequence selected from the group consisting of a nucleotide

sequence coding for any of the amino acid sequences as described in claim 11 and an anti sense nucleotide sequence that is complementary thereto.

15. A plasmid comprising any of the nucleotide sequences described in any  
5 of the  
claims 12, 13 or 14.

16. A vector comprising any of the nucleotide sequences described in any of  
the claims 12, 13 or 14.

10 17. A (micro)organism or cell line in which any of the nucleotide sequences  
described in claim 12 was introduced.

18. A (micro)organism or cell line in which any of the nucleotide sequences  
15 described in claim 13 was introduced.

19. A (micro)organism or cell line in which any of the nucleotide sequences  
described in claim 14 was introduced.

20 20. A process for producing sphingomyelin synthase comprising the  
expression of  
any one of the nucleotide sequences described in claim 12 in a (micro)organism  
or cell line of claim 17 and the isolation of sphingomyelin synthase.

25 21. A process for producing sphingomyelin comprising the expression of the  
nucleotide sequences described in claim 12 in a (micro)organism or cell of claim  
17 and the isolation of sphingomyelin.

22. Use of one of more of the nucleotide sequences of claim 12 to influence  
30 the reaction



*in vivo or in vitro.*

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23. Use of one or more of the nucleotide sequences of claim 12 to identify or develop compounds influencing the reaction

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*in vivo or in vitro.*

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24. A process for producing ethanolamine phosphorylceramide synthase comprising the expression of any one of the nucleotide sequences described in claim 13 in a (micro)organism or cell line of claim 18 and the isolation of ethanolamine phosphorylceramide synthase.

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25. A process for producing ethanolamine phosphorylceramide comprising the

expression of the nucleotide sequences described in claim 13 in a (micro)organism or cell line of claim 18 and the isolation of ethanolamine

25

phosphorylceramide.

26. Use of any one of the nucleotide sequences of claim 13 to influence the reaction

5 CER + PE  $\leftrightarrow$  EPC + DAG

*in vivo or in vitro.*

27. Use of any one of the nucleotide sequences of claim 13 to identify or  
10 develop compounds influencing the reaction

CER + PE  $\leftrightarrow$  EPC + DAG

15 *in vivo or in vitro.*

28. The application of the compounds of claim 23 or 27 in medical use.

29. The application of the compounds of claim 28 for the manufacture  
20 of medicaments treating a disease selected from the group consisting of cancer, metabolic diseases and diseases caused by parasites.

30. A process for producing phosphatidyl:glycoprotein  
cholinephosphotransferase or phosphatidyl:glycolipid  
25 cholinephosphotransferase comprising the expression of any one of the corresponding nucleotide sequences described in claim 14 in a (micro)organism or a cell line of claim 19 and the isolation of phosphatidyl:glycoprotein  
cholinephosphotransferase or phosphatidyl:glycolipid  
cholinephosphotransferase.  
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31. A process for producing phosphorylcholine-substituted glycoprotein or

phosphorylcholine-substituted glycolipid comprising the expression of the corresponding nucleotide sequences described in claim 14 in a (micro)organism or cell of claim 19 and the isolation of phosphorylcholine-substituted glycoprotein or

5 phosphorylcholine-substituted glycolipid .

32. Use of one of more of the nucleotide sequences of claim 14 to influence the reaction

10 glyco lipid/protein + PC  $\leftrightarrow$  PC-substituted glyco lipid/protein + DAG

*in vivo or in vitro.*

33. Use of one of more of the nucleotide sequences of claim 14 to identify or  
15 develop compounds influencing the reaction

glyco lipid/protein + PC  $\leftrightarrow$  PC-substituted glyco lipid/protein + DAG

*in vivo or in vitro.*

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34. The application of the compounds of claim 33 in medical use.

35. The application of the compounds of claim 34 for the manufacture of a medicament treating a disease caused by parasitic nematodes.

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36. A process to isolate candidates for functional genes of a previously unidentified enzyme with known activity from a huge database by combining at least four characteristics based on data from bio-informatics and from biochemistry, viz.

- presence of a sequence motif shared with previously identified enzymes having a related function
- biochemical function of the gene should be unknown until now
- no structural homologues in an organism that does not contain the enzyme
- 5 – ability to mediate a reaction catalysed by the unidentified enzyme upon its heterologous expression in an organism or cell lacking said enzyme activity.

37. A process to isolate candidates for functional genes according to claim 36 characterized by also considering the presence or non-presence of  
10 transmembrane domains depending on the working mechanism of the enzyme in relation to the membrane.

38. A method for determining whether a compound is capable of modulating an enzymatic activity displayed by a cell, said activity comprising  
15 an activity of an enzyme of the group of enzymes identified as sphingomyelin synthases, ethanolamine phosphorylceramide synthases, phosphatidylcholine:glycoprotein cholinephosphotransferase and phosphatidylcholine:glycolipid cholinephosphotransferase, said method comprising providing said cell with a nucleic acid encoding a polypeptide  
20 according to any one of claims 1-11, contacting said cell with said compound and determining whether said enzymatic activity is modulated.

39. A method according to claim 38 wherein said cell is deficient in sphingomyelin synthase activity.  
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40. A method according to claim 38 or claim 39, wherein said cell is a cell of a eukaryotic micro-organism.

41. A method according to claim 40, wherein said cell is yeast cell.  
30

42. A method according to any one of claims 38-41, wherein said polypeptide comprises a sequence as depicted in figure 8 or a functional part, derivative and/or homologue thereof.
- 5 43. A method according to claim 42, wherein said polypeptide comprises a sequence as depicted in figure 8A or a functional part, derivative and/or homologue thereof.
44. A method according to any one of claims 38-43, wherein said  
10 polypeptide is derived from a plasmodium.
45. A method according to claim 44, wherein said plasmodium sequence is a sequence as depicted in figure 8B or a functional part, derivative and/or homologue thereof.
- 15 46. A method according to any one of claims 38-45, wherein said compound comprises RNA.
47. Use of a nucleic acid encoding a polypeptide according to any one of  
20 claims 1-11, as a probe.
48. Use of an oligonucleotide specific for a nucleic acid sequence encoding a polypeptide as depicted in figure 8 or a functional part, derivative and/or homologue thereof, for detecting said sequence.
- 25 49. Use according to claim 47 or claim 48, for assessing whether a cell comprises sphingomyelin synthase activity.
50. Use of an inhibitor of a sphingomyelin synthase according to any one  
30 of claims 1-11, as a cell death promoter.



51. Use according to claim 50, wherein said cell is a cell of a parasite.

52. Use according to claim 50, wherein said cell is a human cell,  
5 preferably a tumor cell.

53. Use of a nucleic acid according to any one of claims 12-14, preferably  
comprising a nucleic acid sequence encoding a polypeptide as depicted in figure  
8 or a functional part, derivative and/or homologue thereof for enhancing cell  
10 survival and/or cell growth.

54. A method for at least in part improving the yield of an secretion  
product of a cell comprising providing said cell with a polypeptide according to  
any one of claims 1-11, or a nucleic acid according to any one of claims 12-14,  
15 preferably comprising a nucleic acid sequence encoding a polypeptide as  
depicted in figure 8 or a functional part, derivative and/or homologue thereof.

55. A method according to claim 54, wherein said cell is a cell of a  
eukaryotic micro-organism.

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56. A method according to any one of claims 38-46, further comprising  
providing said cell or a fraction thereof with a labelled substrate for said  
sphingomyelin synthase.

25 57. A method according to claim 56, further comprising harvesting  
sphingolipid from said cell or said fraction and detecting labelled sphingolipid.

58. A method according to claim 56 or 57, further comprising detecting  
said labelled sphingolipid using (thin layer) chromatography or mass  
30 spectrometry.

59. A method for targeting a first polypeptide according to any one of claims 1-11 to a different cellular compartment comprising providing a cytosolic part of said first polypeptide with a cellular compartment localization  
5 signal of a cytosolic part of a second polypeptide according to any one of claims 1-11, wherein said first and said second polypeptide, when unmodified, reside in different cellular compartments.

60. A method according to claim 59, wherein said cytosolic part of said  
10 first polypeptide comprises the C-terminal end of said polypeptide.

61. A method according to claim 59 or claim 60, wherein said cytosolic part of said second polypeptide comprises the C-terminal end of said polypeptide.  
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62. A method according to any one of claims 59-61, wherein said cellular compartments comprises the plasma membrane, the endosomal compartment, the Golgi, the endoplasmatic reticulum or a combination thereof.

20 63. A method according to any one of claims 59-62, wherein said cellular compartment localization signal of said second polypeptide replace the C-terminal cytosolic part of said first polypeptide.